REMARKS

Claims 1, 3, 5, 17 and 23-25 are pending in the instant specification. Applicants have amended claims 1, 3, 5 and 17. Support for the amendment to claim 3 can be found, for example, on page 5, lines 31-32 of the instant specification. Applicants have added claims 23-25. Support for claim 23 can be found, for example, in claim 2 as filed, and on page 25, line 15, page 28, lines 7 and 28-29, page 29, lines 5 and 29-30, page 30, lines 8-9 and page 31, lines 5-16 of the instant specification. Support for claims 24 and 25 can be found in claims 1 and 5 as filed. Applicants have canceled claims 2, 4, 6-16 and 18-22 for being drawn to non-elected subject matter and reserve the right to pursue these claims in a divisional application. Applicants have amended the specification to delete reference to hyperlinks, correct typographical errors and to correct a priority claim. No new matter is added.

Specification

The Examiner objected to the specification, on page 5 of the Office Action, because it contained embedded hyperlinks on pages 23 and 32. Applicants have deleted these hyperlinks, thereby overcoming this objection.

The Examiner also objected to the specification, on page 5 of the Office Action, because on page 32, lines 5-7, it refers to Figures 1-3 as containing DNA sequences. As indicated by the Examiner, the recited DNA sequences appear in Figures 3-5. Applicants have amended the specification to remedy this typographical error, thus overcoming this objection.

Priority

The Examiner objected to the priority claim, on pages 5-6 of the Office Action, because it did not contain a specific reference for the priority claim between U.S. Application No. 09/345,217 and International Application No. PCT/GB98/01481. The Examiner asserted that 09/345,217 was a national stage entry of PCT/GB98/01481 and that the priority claim should be amended to indicate this.

Applicants reviewed PAIR and the file of U.S. Application No. 09/345,217. While PAIR indicates that U.S. Application No. 09/345,217 is a national stage entry of International Application No. PCT/GB98/01481, the file shows that it is a continuation under 35 U.S.C. 111(a) and 37 CFR 1.53(b). Applicants have amended the priority claim to indicate this.

Claim Rejections

35 U.S.C. §112, Second Paragraph

The Examiner has rejected claims 3 and 17, on page 6 of the Office Action, under 35 U.S.C. §112, second paragraph, for indefiniteness. The Examiner asserted that claim 3 was indefinite for reciting a list of allele detection techniques as detecting means and for lack of antecedent basis for the phrase "detecting means". The Examiner asserted that claim 17 was indefinite for reciting the word "corresponding".

Applicants have amended claim 3 to eliminate reference to the list of allele detection techniques in claim 3 as "detecting means". Also, Applicants have amended the phrase "detecting means" to recite only the word "means". Applicants have also amended claim 17 to delete the word "corresponding". In light of these amendments, Applicants submit that claims 3 and 17 are definite and request that this rejection be withdrawn.

Double Patenting

The Examiner has rejected claims 1, 3, 5 and 17, on pages 8-9 of the Office Action, under the judicially created doctrine of obviousness-type double patenting over claims 1-5 of Duff *et al.* U.S. Patent No. 6,713,253. The Examiner asserted that claims 1-5 teach means of detecting IL-1B -511 allele 1 or 2. Applicants traverse this rejection.

Claims 1-5 of U.S. Patent No. 6,713,253 teach a method of increased risk of sight threatening diabetic retinopathy by detecting a polymorphism pattern comprising an IL-1RN (VNTR) allele 1, an IL-1B -511 allele 2 or an IL-1A -889 allele 2 in a nucleic acid sample from a patient. Applicants have amended claims 1 and 5 from which claims 3 and 17 depend, to stipulate that the kits must contain a means for detecting IL-1B -511 allele 1 or 2 and means of detecting an allele selected from the group consisting of: allele 2 of 1731 IL-RN, allele 2 of 1812 IL-1RN, allele 2 of 1868 IL-1RN, allele 2 of 1887 IL-1RN, allele 2 of 8006 IL-1RN, allele 2 of 8061 IL-1RN, allele 2 of 9589 IL-1RN, allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 2 of the VNTR

marker of IL-1RN. Claims 1-5 of U.S. Patent No. 6,713,253 do not teach or suggest the limitations added to instant claims 1, 3, 5 and 17 as amended, herein. Thus, Applicants submit that instant claims 1, 3, 5 and 17 are not obvious in light of claims 1-5 of U.S. Patent No. 6,713,253, and request that this rejection be withdrawn.

The Examiner has also rejected claims 1, 3, 5 and 17, on pages 9-10 of the Office Action, under the judicially created doctrine of obviousness-type double patenting over claims 1-6 of Kornman *et al.* U.S. Patent No. 6,733,967. The Examiner asserted that claims 1-6 teach means of detecting IL-1B -511 allele 1 or 2. Applicants traverse this rejection.

Claims 1-6 of U.S. Patent No. 6,733,967 teach a method of determining whether a female subject is predisposed to having a low birthrate by detecting an IL-1B -511 allele 2 in a nucleic acid sample from a patient. Applicants have amended claims 1 and 5 from which claims 3 and 17 depend, to stipulate that the kits must contain a means for detecting IL-1B -511 allele 1 or 2 and means of detecting an allele selected from the group consisting of: allele 2 of 1731 IL-RN, allele 2 of 1812 IL-1RN, allele 2 of 1868 IL-1RN, allele 2 of 1887 IL-1RN, allele 2 of 8006 IL-1RN, allele 2 of 8061 IL-1RN, allele 2 of 9589 IL-1RN, allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 2 of the VNTR marker of IL-1RN. Claims 1-6 of U.S. Patent No. 6,733,967 do not teach or suggest the limitations added to instant claims 1, 3, 5 and 17 as amended, herein. Thus, Applicants submit that instant claims 1, 3, 5 and 17 are not obvious in light of claims 1-6 of U.S. Patent No. 6,733,967, and request that this rejection be withdrawn.

The Examiner has also rejected claims 1, 3, 5 and 17, on page 10 of the Office Action, under the judicially created doctrine of obviousness-type double patenting over claims 1-15 of Duff *et al.* U.S. Patent No. 6,140,047. The Examiner asserted that claims 1-15 teach means of detecting IL-1B -511 alleles 1 and 2. Applicants traverse this rejection.

Claims 1-15 of U.S. Patent No. 6,140,047 teach a kit which includes PCR primers which may be used to detect a IL-1B -511 allele 2 in a nucleic acid sample from a patient. Applicants have amended claims 1 and 5 from which claims 3 and 17 depend, to stipulate that the kits must contain a means for detecting IL-1B -511 allele 1 or 2 and means of detecting an allele selected from the group consisting of: allele 2 of 1731 IL-RN, allele 2 of 1812 IL-1RN, allele 2 of 1868 IL-1RN, allele 2 of 1887 IL-1RN, allele 2 of 8006 IL-1RN, allele 2 of 8061 IL-1RN, allele 2 of 9589 IL-1RN, allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 2 of the VNTR marker of IL-1RN. Claims 1-15 of U.S. Patent No. 6,140,047 do not teach or suggest the limitations added to instant claims 1, 3, 5 and 17 as amended, herein. Thus, Applicants submit that instant claims 1, 3, 5 and 17 are not obvious in light of claims 1-15 of U.S. Patent No. 6,140,047, and request that this rejection be withdrawn.

The Examiner has also rejected claims 1, 3, 5 and 17, on page 11 of the Office Action, under the judicially created doctrine of obviousness-type double patenting over claims 1-9 of Kornman *et al.* U.S. Patent No. 5,686,246. The Examiner asserted that claims 1-9 teach means of detecting IL-1B -511 alleles 1 and 2. Applicants traverse this rejection.

Claims 1-9 of U.S. Patent No. 5,686,246 teach a method of predicting a patient's susceptibility to increased severity of periodontal disease or severe periodontal disease by detecting an IL-1A allele 2 and an IL-1B allele 2. Applicants have amended claims 1 and 5 from which claims 3 and 17 depend, to stipulate that the kits must contain a means for detecting IL-1B -511 allele 1 or 2 and means of detecting an allele selected from the group consisting of: allele 2 of 1731 IL-RN, allele 2 of 1812 IL-1RN, allele 2 of 1868 IL-1RN, allele 2 of 1887 IL-1RN, allele 2 of 8006 IL-1RN, allele 2 of 8061 IL-1RN, allele 2 of 9589 IL-1RN, allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223

marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 2 of the VNTR marker of IL-1RN. Claims 1-9 of U.S. Patent No. 5,686,246 do not teach or suggest the limitations added to instant claims 1, 3, 5 and 17 as amended, herein. Claims 1-9 of U.S. Patent No. 5,686,246 teach only the detection of allele 2 of an IL-1A and an IL-1B gene, not the detection of the alleles described in instant claims 1, 3, 5 and 17 as amended, herein. Thus, Applicants submit that instant claims 1, 3, 5 and 17 are not obvious in light of claims 1-9 of U.S. Patent No. 5,686,246, and request that this rejection be withdrawn.

The Examiner has also rejected claims 1, 3, 5 and 17, on pages 11-12 of the Office Action, under the judicially created doctrine of obviousness-type double patenting over claims 1-15 of Francis *et al.* U.S. Patent No. 6,210,877. The Examiner asserted that claims 1-15 teach means of detecting IL-1B -511 alleles 1 and 2. Applicants traverse this rejection.

Claims 1-15 of U.S. Patent No. 6,210,877 teach a method of determining a patient's predisposition to coronary artery disease by detecting IL-1B -511 allele 2. Applicants have amended claims 1 and 5 from which claims 3 and 17 depend, to stipulate that the kits must contain a means for detecting IL-1B -511 allele 1 or 2 and means of detecting an allele selected from the group consisting of: allele 2 of 1731 IL-RN, allele 2 of 1812 IL-1RN, allele 2 of 1868 IL-1RN, allele 2 of 1887 IL-1RN, allele 2 of 8006 IL-1RN, allele 2 of 8061 IL-1RN, allele 2 of 9589 IL-1RN, allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 2 of the VNTR marker of IL-1RN. Claims 1-15 of U.S. Patent No. 6,210,877 do not teach or suggest the limitations added to instant claims 1, 3, 5 and 17 as amended, herein. Thus, Applicants submit that instant claims 1, 3, 5 and 17 are not obvious in light of claims 1-15 of U.S. Patent No. 6,210,877, and request that this rejection be withdrawn.

The Examiner has also rejected claims 1, 3, 5 and 17, on pages 12-13 of the Office Action, under the judicially created doctrine of obviousness-type double patenting over claims 1-49 of Duff *et al.* U.S. Patent No. 6,746,839. The Examiner asserted that claims 1-49 teach means of detecting IL-1B -511 alleles 1 and 2. Applicants traverse this rejection.

Claims 1-49 of U.S. Patent No. 6,746,839 teach a method of determining whether a patient is predisposed to developing obstructive airway disease by detecting a number of alleles which may also include the allele 2 of IL-1B -511. Applicants have amended claims 1 and 5 from which claims 3 and 17 depend, to stipulate that the kits must contain a means for detecting IL-1B -511 allele 1 or 2 and means of detecting an allele selected from the group consisting of: allele 2 of 1731 IL-RN, allele 2 of 1812 IL-1RN, allele 2 of 1868 IL-1RN, allele 2 of 1887 IL-1RN, allele 2 of 8006 IL-1RN, allele 2 of 8061 IL-1RN, allele 2 of 9589 IL-1RN, allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 2 of the VNTR marker of IL-1RN. Claims 1-49 of U.S. Patent No. 6,746,839 do not teach or suggest the limitations added to instant claims 1, 3, 5 and 17 as amended, herein. Thus, Applicants submit that instant claims 1, 3, 5 and 17 are not obvious in light of claims 1-49 of U.S. Patent No. 6,746,839, and request that this rejection be withdrawn.

The Examiner has also rejected claims 1, 3, 5 and 17, on page 13 of the Office Action, under the judicially created doctrine of obviousness-type double patenting over claims 1-7 of Duff *et al.* U.S. Patent No. 6,268,142. The Examiner asserted that claims 1-7 teach means of detecting IL-1B -511 alleles 1 and 2. Applicants traverse this rejection.

Claims 1-7 of U.S. Patent No. 6,268,142 teach a method of determining a patient is predisposed to a disease associated with the IL-1 inflammatory haplotype by detecting a number of alleles which may also include the alleles of IL-1B -511. Applicants have amended claims 1 and 5 from which claims 3 and 17 depend, to stipulate that the kits must contain a means for detecting IL-1B -511 allele 1 or 2 and means of detecting an allele selected from the group consisting of: allele 2 of 1731 IL-RN, allele 2 of 1812 IL-1RN, allele 2 of 1868 IL-1RN, allele 2

of 1887 IL-1RN, allele 2 of 8006 IL-1RN, allele 2 of 8061 IL-1RN, allele 2 of 9589 IL-1RN, allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 2 of the VNTR marker of IL-1RN. Claims 1-7 of U.S. Patent No. 6,268,142 do not teach or suggest the limitations added to instant claims 1, 3, 5 and 17 as amended, herein. Thus, Applicants submit that instant claims 1, 3, 5 and 17 are not obvious in light of claims 1-7 of U.S. Patent No. 6,268,142, and request that this rejection be withdrawn.

The Examiner has also rejected claims 1, 3, 5 and 17, on page 14 of the Office Action, under the judicially created doctrine of obviousness-type double patenting over claims 1-7 of di Giovine *et al.* U.S. Patent No. 6,251,598. The Examiner asserted that claims 1-7 teach means of detecting IL-1B -511 alleles 1 and 2. Applicants traverse this rejection.

Claims 1-7 of U.S. Patent No. 6,251,598 teach a method of predicting the severity with which an infected a subject is likely to develop sepsis by detecting linkage disequilibrium between IL-1B -511 allele 2 and an allele in the IL-1B promoter. Applicants have amended claims 1 and 5 from which claims 3 and 17 depend, to stipulate that the kits must contain a means for detecting IL-1B -511 allele 1 or 2 and means of detecting an allele selected from the group consisting of: allele 2 of 1731 IL-RN, allele 2 of 1812 IL-1RN, allele 2 of 1868 IL-1RN, allele 2 of 1887 IL-1RN, allele 2 of 8006 IL-1RN, allele 2 of 8061 IL-1RN, allele 2 of 9589 IL-1RN, allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 2 of the VNTR marker of IL-1RN. Claims 1-7 of U.S. Patent No. 6,251,598 do not teach or suggest the limitations added to instant claims 1, 3, 5

and 17 as amended, herein. Thus, Applicants submit that instant claims 1, 3, 5 and 17 are not obvious in light of claims 1-7 of U.S. Patent No. 6,251,598, and request that this rejection be withdrawn.

The Examiner has also rejected claims 1, 3, 5 and 17, on pages 14-15 of the Office Action, under the judicially created doctrine of obviousness-type double patenting over claims 1-6 of Duff *et al.* U.S. Patent No. 6,706,478. Applicants traverse this rejection..

Claims 1-6 of U.S. Patent No. 6,706,478 teach a method of detecting whether a subject is suffering from or is predisposed to developing a disease or condition associated with an IL-1 inflammatory haplotype by, in part, detecting the presence of IL-1B -511 allele 2. Applicants have amended claims 1 and 5 from which claims 3 and 17 depend, to stipulate that the kits must contain a means for detecting IL-1B -511 allele 1 or 2 and means of detecting an allele selected from the group consisting of: allele 2 of 1731 IL-RN, allele 2 of 1812 IL-1RN, allele 2 of 1868 IL-1RN, allele 2 of 1887 IL-1RN, allele 2 of 8006 IL-1RN, allele 2 of 8061 IL-1RN, allele 2 of 9589 IL-1RN, allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 1 of the -511 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, allele 2 of +4845 of IL-1A, and allele 2 of the VNTR marker of IL-1RN. Claims 1-6 of U.S. Patent No. 6,706,478 do not teach or suggest the limitations added to instant claims 1, 3, 5 and 17 as amended, herein. Thus, Applicants submit that instant claims 1, 3, 5 and 17 are not obvious in light of claims 1-6 of U.S. Patent No. 6,706,478, and request that this rejection be withdrawn.

The Examiner has provisionally rejected claims 1, 3, 5 and 17, on pages 15-16 of the Office Action, under the judicially created doctrine of obviousness-type double patenting over claims 1-21 of U.S. Application No. 10/914,396. Applicants will revisit this provisional rejection when claims are rendered allowable in either case.

The Examiner has also provisionally rejected claims 1, 3, 5 and 17, on pages 16-17 of the Office Action, under the judicially created doctrine of obviousness-type double patenting over claims 1-19 of U.S. Application No. 11/283,168. Applicants will revisit this provisional rejection when claims are rendered allowable in either case.

The Examiner has also provisionally rejected claims 1, 3, 5 and 17, on pages 17-18 of the Office Action, under the judicially created doctrine of obviousness-type double patenting over claims 1-9 of U.S. Application No. 10/838,503. Applicants will revisit this provisional rejection when claims are rendered allowable in either case.

35 U.S.C. §102

The Examiner has rejected claims 1, 3, 5 and 17, on pages 18-19 of the Office Action, under 35 U.S.C. § 102(a) and (e) for being anticipated by Kornman *et al.* U.S. Patent No. 5,686,246 ("Kornman"). The Examiner alleged that Kornman teaches primers used for detection of IL-1B -511 alleles 1 and 2 and kits containing the same.

Applicants have amended claims 1 and 5 from which claims 3 and 17 depend, to stipulate that the kits must contain a means for detecting IL-1B -511 allele 1 or 2 and means of detecting an allele selected from the group consisting of: allele 2 of 1731 IL-RN, allele 2 of 1812 IL-1RN, allele 2 of 1868 IL-1RN, allele 2 of 1887 IL-1RN, allele 2 of 8006 IL-1RN, allele 2 of 8061 IL-1RN, allele 2 of 9589 IL-1RN, allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, and allele 2 of +4845 of IL-1A. Kornman does not teach the limitations of claims 1, 3, 5 and 17 as amended and therefore cannot anticipate these claims. Thus, Applicants request that this rejection be withdrawn.

The Examiner has also rejected claims 1, 3, 5 and 17, on pages 19-21 of the Office Action, under 35 U.S.C. § 102 (e) for being anticipated by Francis *et al.* U.S. Patent No. 6,210,877 ("Francis"). The Examiner alleged that Francis teaches primers used for detection of IL-1B -511 alleles 1 and 2 and kits containing the same.

As explained above, Applicants have amended claims 1 and 5 from which claims 3 and 17 depend, to stipulate that the kits must contain a means for detecting IL-1B -511 allele 1 or 2 and means of detecting an allele selected from the group consisting of: allele 2 of 1731 IL-RN, allele 2 of 1812 IL-1RN, allele 2 of 1868 IL-1RN, allele 2 of 1887 IL-1RN, allele 2 of 8006 IL-1RN, allele 2 of 8061 IL-1RN, allele 2 of 9589 IL-1RN, allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of +2018 of IL-1RN, and allele 2 of +4845 of IL-1A. Francis does not teach the limitations of claims 1, 3, 5 and 17 as amended and therefore cannot anticipate these claims. Thus, Applicants request that this rejection be withdrawn.

The Examiner has also rejected claims 1, 3, 5 and 17, on pages 21-22 of the Office Action, under 35 U.S.C. § 102 (e) for being anticipated by Mansfield *et al.* Gastroenterology 196:637-642 (1994) ("Mansfield"). The Examiner alleged that Mansfield teaches primers used for detection of IL-1B -511 alleles 1 and 2 and kits containing the same.

As explained above, Applicants have amended claims 1 and 5 from which claims 3 and 17 depend, to stipulate that the kits must contain a means for detecting IL-1B -511 allele 1 or 2 and means of detecting an allele selected from the group consisting of: allele 2 of 1731 IL-RN, allele 2 of 1812 IL-1RN, allele 2 of 1868 IL-1RN, allele 2 of 1887 IL-1RN, allele 2 of 8006 IL-1RN, allele 2 of 8061 IL-1RN, allele 2 of 9589 IL-1RN, allele 4 of the 222/223 marker of IL-1A, allele 4 of the gz5/gz6 marker of IL-1A, allele 1 of the -889 marker of IL-1A, allele 1 of the +3954 marker of IL-1B, allele 3 of the gaat.p33330 marker, allele 3 of the Y31 marker, allele 2 of +2018 of IL-1RN, allele 1 of +4845 of IL-1A, allele 3 of the 222/223 marker of IL-1A, allele 3 of the gz5/gz6 marker of IL-1A, allele 2 of the -889 marker of IL-1A, allele 2 of the +3954 marker of IL-1B, allele 4 of the gaat.p33330 marker, allele 6 of the Y31 marker, allele 1 of

+2018 of IL-1RN and allele 2 of +4845 of IL-1A. Mansfield does not teach the limitations of claims 1, 3, 5 and 17 as amended and therefore cannot anticipate these claims. Thus, Applicants request that this rejection be withdrawn.

CONCLUSION

A favorable action on the merits is respectfully requested. If further discussion of this case is deemed helpful, the Examiner is encouraged to contact the undersigned at the telephone number provided below, and is assured of full cooperation in progressing the instant claims to allowance.

Respectfully submitted,

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